

A Retrospective Study of Histopathology and Clinical Correlation of Renal Cell Carcinoma in a Tertiary Medical College, India

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ABSTRACT

Background: The study was conducted to understand the clinical solution of renal cell carcinoma. Correlation was done by clinical presentation with radiological features and histopathology of renal cell carcinoma. The stress upon to understand the necessity for a team-approach between Clinician, Radiologist and Pathologist and vice versa is emphasized. **Aim:** Histopathology and Clinical Correlation of Renal cell carcinoma. **Methods:** The total number of renal tumours studied during the 8 years period was 45 cases among which 25 cases were diagnosed by histopathology as various types of renal cell carcinoma conclusively. This is a retrospective study of renal tumours, diagnosed by histopathology as various types of renal cell carcinoma. All the relevant clinical data of the patients were searched from the ward records. The various Radiological features were collected. **Results:** The total number of renal tumours studied during the 8 years period was 45 cases among which 25 cases were diagnosed by histopathology as various types of renal cell carcinoma conclusively. MRI provides molecular information with regard to renal cell carcinoma and potentially aid in biopsy planning. The total cases reported in the department is twenty five vases out of which sixteen cases are attending follow up after 3 years. **Conclusion:** The Fuhrman grading of renal cell carcinoma correlated grading of renal cell carcinoma. Preoperative radiological classification can be used as a supplement to the histopathological grading. Renal cell carcinoma needs correlation between Radiologist, Pathologist and Clinician.

Keywords: Papillary renal cell carcinoma, Multidetector computed tomography, Clear cell renal cell carcinoma, Magnetic resonance imaging, Chromophobe renal cell carcinoma, Tumor staging (TNM), and Treatment protocols.

INTRODUCTION

Representing 2%-3% of adult cancers, renal cell carcinoma (RCC) accounts for 90% of renal malignancies and is the most lethal neoplasm of the urologic system. Renal cell carcinoma (RCC) is a kidney cancer that originates in the lining of the proximal convoluted tubule, The 2004 World Health Organization Classification of adult renal tumors stratifies RCC into several distinct histologic subtypes of which clear cell, papillary and chromophobe tumors account for 70%, 10%-15%, and 5%, respectively. Renal cell carcinoma (RCC) accounts for 90% of adult renal malignancies and is the most lethal of all urologic cancers.^[1-3] RCC is not a single entity but rather a heterogeneous group of neoplasms with varying histological findings,

cytogenetic abnormalities, biologic behaviour, prognosis and response to therapy.^[1,4-10] Chromosome 3p deletions are found in up to 96% of clear cell RCCs including somatic inactivating mutations of the Von Hippel-Lindau (VHL) gene.^[11,12] Cytogenetic abnormalities are associated with the papillary subtype include trisomies of chromosomes 3, 7, 12, 16, 17 and 20, c-MET mutations and loss of the Y chromosome.^[11,13,14] Cytogenetic abnormalities associated with chromophobe RCC include loss of multiple chromosomes such as 1, 2, 6, 10, 13, 17 and 21.^[15] The clear cell subtype shows a less favourable outcome compared with papillary and chromophobe subtypes, and is more likely to be symptomatic, present at an advanced stage, and show a greater propensity to metastasize.^[1,4-6,8,9,11,16] The 5-year survival rate is 44%-69% in clear cell tumors, 82%-92% in papillary tumors and 78%-92% in chromophobe tumors.^[6-10,17] In advanced disease, a tailored management approach is recommended as the effectiveness of systemic therapy including the specific regime used may be influenced by the RCC subtype.^[5,18-22] Studies have suggested that clear cell,

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papillary and chromophobe subtypes can be differentiated non-invasively on imaging[1]. Studies have also found that RCCs that develop in patients with end-stage renal disease (ESRD) tend to be less aggressive than RCCs that occur in the general population.^[30-32] Hereditary RCCs account for 4% and show a predilection towards early-onset, bilaterality and multicentricity.^[32] Around 25% to 60% of VHL patients develop RCC with the risk of metastasis related to tumor size.^[33-35] Birt-Hogg-Dube syndrome, an autosomal dominant condition caused by mutations in the folliculin gene, predisposes to cutaneous tumors, oncocytomas and clear cell, papillary and chromophobe RCCs.^[36,37] Recently, it has been discovered that patients with hereditary succinate dehydrogenase mutations are at risk of developing aggressive early-onset RCCs in addition to pheochromocytomas and paraganglioma.^[38] Most RCCs are asymptomatic and discovered as unexpected findings on imaging performed for unrelated clinical indications.^[39-42] The classic triad of a palpable mass, flank pain and haematuria is found in 6%-10% and portends a more aggressive histology and advanced disease.^[43,44] Clear cell RCC typically shows a heterogeneous consistency (secondary to necrosis, cystic change or hemorrhage), has high signal intensity on T2-weighted magnetic resonance imaging (MRI), and is hypervascular on dynamic contrast-enhanced computed tomography or MRI examinations. Most papillary RCCs are detected while at a low grade and small size, show low signal intensity on T2-weighted MRI, and are hypovascular following contrast administration. Chromophobe RCCs may have a homogeneous solid appearance even when large, and may exhibit a central stellate scar and spoke-wheel enhancement. Clear cell RCC typically exhibits exophytic growth and has a tendency to be heterogeneous due to intratumoral necrosis, cystic change or hemorrhage. Interruption of the tumor capsule has also been correlated with high tumor grade.^[45] Cystic papillary RCCs may show haemorrhagic fluid content and internal mural nodules or papillary projections while cystic clear cell RCCs typically show clear fluid content and irregular walls and septations.^[46] Chromophobe RCC tends to appear well-circumscribed and homogeneous (cystic change and necrosis are uncommon) even when large, and perinephric infiltration and vascular involvement (< 4%) are rare.^[1,11] Most papillary RCCs demonstrate low T2 signal intensity.^[47,48] In contrast, most clear cell RCCs show high T2 signal intensity.^[11,49,50] Several preliminary studies have shown encouraging results in utilizing diffusion-weighted imaging (DWI) for characterizing RCCs into its main subtypes as well as into high grade and low grade tumors.^[51-54] DWI has been used to differentiate various subgroups of renal masses. MRI is also useful for imaging renal vein and IVC tumour thrombus and the rostral

extension (important in preoperative planning). The presence of enhancement in the thrombus is able to distinguish between bland and tumour thrombus.

Fuhrman et al Grading of Renal Cell carcinoma:

Specifically, grade I tumours consist of cells with small (approximately 10 mm), round, uniform nuclei with inconspicuous or absent nucleoli; grade II tumours have larger nuclei (approximately 15 mm) with irregular morphology and small nucleoli when examined under high power (400 magnification); grade III tumours have even larger nuclei (approximately 20 mm) with irregular outlines and large, prominent nucleoli that are evident even at low power (100 magnification); and grade IV tumours differ from grade III lesions in that they contain bizarre, multilobed nuclei and heavy chromatin clumps.

Table 1: Staging Based on TNM staging system

The staging of renal cell carcinoma is the most important factor in predicting its prognosis. Staging can follow the TNM staging system, where the size and extent of the tumour (T), involvement of lymph nodes (N) and metastases (M) are classified separately. Also, it can use overall stage grouping into stage I-IV, with the 1997 revision of AJCC described below:^[52]

Stage I	Tumour of a diameter of 7 cm (approx. 2 3/4 inches) or smaller, and limited to the kidney. No lymph node involvement or metastases to distant organs.
Stage II	Tumour larger than 7.0 cm but still limited to the kidney. No lymph node involvement or metastases to distant organs
Stage III any of the following	Tumour of any size with involvement of a nearby lymph node but no metastases to distant organs. Tumour of this stage may be with or without spread to fatty tissue around the kidney, with or without spread into the large veins leading from the kidney to the heart.
	Tumour with spread to fatty tissue around the kidney and/or spread into the large veins leading from the kidney to the heart, but without spread to any lymph nodes or other organs.
Stage IV any of the following	Tumour that has spread directly through the fatty tissue and the fascia ligament-like tissue that surrounds the kidney.
	Involvement of more than one lymph node near the kidney
	Involvement of any lymph node not near the kidney
	Distant metastases, such as in the lungs, bone, or brain.

Surgical and further management:

Stage IA

Partial nephrectomy is a widely accepted treatment for RCC tumors of less than 4 cm in diameter. Nephron-sparing partial nephrectomy - with the objective being the complete surgical extirpation of the tumor while retaining sufficient healthy tissue for adequate renal function - is the preferred treatment option for stage Ia. Over the last decade, the clinical indications for partial nephrectomy have been expanded to include most patients with low stage

tumors as studies have demonstrated that partial nephrectomy is as effective a therapeutic option as radical nephrectomy with comparable rates of tumor-free survival and overall survival.

Stage Ib

The NCCN recommends that either partial nephrectomy or radical nephrectomy be performed for stage Ib tumors.^[2] Both techniques show comparable oncologic control.

Stage II and III

The NCCN recommends that radical nephrectomy be performed for stage II and III tumors.^[2] Routine adrenalectomy and lymphadenectomy is not advocated in the absence of radiologic disease at these sites as it does not improve survival. A laparoscopic approach is favoured for stage II tumors while stage III tumors are usually treated by an open approach.^[47] 1) baseline abdominal CT or MRI within 3-6 months, then CT, MRI or US every 3-6 months for at least 3 years and then annually up to 5 years; (2) baseline chest CT within 3-6 months after surgery with continued imaging (CT or chest X-ray) every 3-6 months for at least 3 years and then annually up to 5 years.

Stage IV

Renal cell cancers are typically treated with both local and systemic therapy. Local therapy consists of surgery to remove the entire affected kidney and any surrounding cancer. The surgery for Stage IV renal cell cancer is called a radical nephrectomy and involves removing the entire affected kidney, the attached adrenal gland, and any adjacent fat and involved lymph nodes or major blood vessels. Systemic therapy is directed at destroying cancer cells throughout the body and may include chemotherapy, targeted therapy, or immunotherapy. A randomized trial by Motzer et al involving 750 patients with metastatic clear cell RCC showed that patients treated with sunitinib had longer progression free survival and overall survival compared with patients treated with interferon- α . Several studies have suggested that VEGF-TKIs may be less effective in treating papillary and chromophobe RCCs compared with clear cell RCCs.^[18,26,49-51] Potential agents include temsirolimus, sorafenib, sunitinib, pazopanib, axitinib, everolimus, bevacizumab or erlotinib. Preliminary studies have suggested that temsirolimus has efficacy in treating papillary RCC. The NCCN guidelines for stage 4 patients are as follows.^[2] (1) Cases that involve a potentially resectable solitary metastatic site should undergo nephrectomy and surgical metastasectomy;

(2) cases that involve a potentially resectable RCC with multiple metastatic sites should undergo cytoreductive nephrectomy in appropriate patients prior to systemic therapy; and (3) cases with medically or surgically unresectable disease should undergo systemic therapy.

The NCCN suggests that stage IV patients should undergo baseline chest, abdominal and pelvic imaging by CT or MRI pre-treatment or prior to observation, followed by repeat imaging every 6-16 weeks as per physician discretion and per patient clinical status.^[22] The imaging frequency may be modified depending on the rate of disease change and the sites of active disease.^[22]

Aim: Histopathology and Clinical Correlation of Renal cell carcinoma

MATERIALS AND METHODS

The total number of renal tumours studied during the 8 years period was 45 cases among which 25 cases were diagnosed by histopathology as various types of renal cell carcinoma conclusively. This is a retrospective study of renal tumours, diagnosed by histopathology as various types of renal cell carcinoma. All the relevant clinical data of the patients were searched from the ward records. The various Radiological features were collected. The clinical features examined included age, gender, smoking history, recent onset hypertension, performance status, and presenting symptoms. A comprehensive health check up on general conditions were taken and stored in the computer server.

RESULTS

Clear cell carcinoma was the most reported case and sixteen cases were reported, other tumours were papillary carcinoma and chromophobe carcinoma in the study covering 8 years period was 45 cases among which 25 cases were diagnosed by histopathology as various types of renal cell carcinoma conclusively at Thoothukudi Medical College. [Table 2]

Table 2: Histopathological Subtypes of Renal cell Carcinoma and corresponding grades

Grades	I	II	III	IV	Total
Types					
Clear cell	10	4	2	0	16
Papillary	3	2	1	0	6
Chromophobe	1	2	0	0	3
Total	14	8	3	0	25

Table 3: Histopathological Age, Sex distribution and Signs, Symptoms and Detailed history in the Subtypes of Renal cell Carcinoma

Tumour type	Age group	M:F Ratio	Signs and Symptoms
Clear cell carcinoma	Females range from 66-74 years	7:9	Ten patients had complaints of fever, haematuria and flank pain. Two

	of age old and the age involved in male was 69-74 years of age old.		patients had haematuria. Four patients had incidental findings.
Papillary carcinoma	Females range from 60-74 years of age old and the age involved in male was 64-75 years of age old.	3:3	Three patients had haematuria. Three patients had incidental findings.
Chromophobe carcinoma	Females range from 62-70 years of age old and the age involved in male was 75 years of age old.	2:1	Two patients had haematuria. One patient had incidental findings.

Table 4: Correlation study of Renal cell Carcinoma

MRI T1 shows often heterogeneous due to necrosis, haemorrhage and solid components T2 shows appearances depend on histology clear cell RCC with hyperintense signal and papillary RCC with hypointense signal. Histopathology section shows clear cell carcinoma with increased vascularity and clear cytoplasm with four grades of Fuhrman nuclei, Papillary renal cell carcinoma showing papillary architecture and chromophobe renal carcinoma showing the neoplastic cells have a fine reticular cytoplasm and bland nuclei some of which have 'raisinoid' appearance

Tumour	Radiographic Findings	Histopathological Findings
Clear cell renal carcinoma		
Grade I	CT scan shows heterogeneously enhancing mass at the upper pole of the right kidney after administration of contrast.	Section studied shows clear cell carcinoma with increased vascularity and clear cytoplasm with features of Fuhrman grade 1 nuclei which are uniform, lack or have inconspicuous nucleoli.
Grade II	Renal cell cancer (RCC) lower pole of left kidney. Arterial (40sec) contrast enhanced CT shows areas of tumour with low intake of contrast surrounded by areas of increased contrast uptake.	Section studied shows clear cell carcinoma with features of tumor cells have mild nuclear pleomorphism with occasional small nucleoli and stippled chromatin typical of Fuhrman grade 2 nuclei.
Grade III	An arterial phase CT will show enhancement of a tumour thrombus due to neovascularisation of the tumour, as in this case.	Section studied shows clear cell carcinoma with features of Fuhrman grade 3 nuclei, patchy, and show moderate pleomorphism and large nucleoli.
Grade IV	Left heterogenous enhancing mass in the mid-pole of the left kidney. This is well illustrated on this 4 phase renal angiogram CT study.	The marked nuclear enlargement of grade 4 nuclei is obvious when compared to the scattered inflammatory cells. Prominent cherry-red nucleoli, with some nuclei harbouring two or three nucleoli,
Papillary renal cell carcinoma		
Grade I	A well circumscribed, 31mm diameter, lesion is identified along the supero-posterior cortical pole of the right kidney. It extends deep towards the calyceal system.	Section studied shows papillary carcinoma with features of numerous papillae. Note the nuclei are small, have open chromatin and indistinct nucleoli typical of type 1 papillary renal cell carcinoma.
Grade II	Left heterogenous enhancing mass in the mid-pole of the left kidney. This is well illustrated on this 4 phase renal angiogram CT study.	Section studied shows papillary carcinoma a tumour composed of several tubulo-papillary structures. There is nuclear enlargement and hyperchromasia, prominent nucleoli and more abundant basophilic cytoplasm.
Chromophobe renal carcinoma	CT shows a 5 cm right renal mass lesion isodense to renal parenchyma. Weak contrast enhancement from 40 to 50 HU on the average.	Section studied shows the neoplastic cells have a fine reticular cytoplasm and bland nuclei some of which have 'raisinoid' appearance. The cells have distinct, thick nuclear membranes and perinuclear halos.

RCC with heterogenous enhancement
Normal kidney with uniform contrast enhancement



Figure 1: CT scan shows heterogeneously enhancing mass at the upper pole of the right kidney after administration of contrast.

Uniform nuclei
Clear cytoplasm

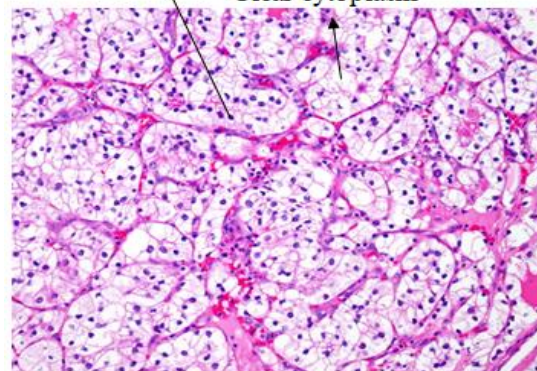


Figure 2: Section studied shows small uniform nuclei with evenly distributed chromatin and the absence of nucleoli, all of which are features of Fuhrman grade 1 nuclei.

Clear Cell Renal Cell Carcinoma

Clear cell renal carcinoma is derived from the proximal convoluted tubule. Frequency 60-70%. Most commonly affects male patients in their sixties and seventies. Microscopically the tumor cells are large, the appearance of the cytoplasm ranging from optically clear, with sharply outlined boundaries. Clear cell renal carcinoma (conventional) arises from proximal convoluted tubules large uniform cells with clear cytoplasm highly vascular. Based on nuclear features these tumour is graded into four grades. Fuhrman grade 1 nuclei which are uniform, lack or have inconspicuous nucleoli. The tumor cells have mild nuclear pleomorphism with occasional small nucleoli and stippled chromatin typical of Fuhrman grade 2 nuclei. Fuhrman grade 3 nuclei, may be patchy, show moderate pleomorphism and large nucleoli. The marked nuclear enlargement of grade 4 nuclei is obvious when compared to the scattered inflammatory cells. Prominent cherry-red nucleoli, with some nuclei harbouring two or three nucleoli. Sixteen cases clear cell renal carcinoma of were reported. Nine cases involving females and seven case involving males. The age group involved in females range from 66-74 years of age old and the age involved in male was 69-74 years of age old. Clear Cell Renal Cell Carcinoma

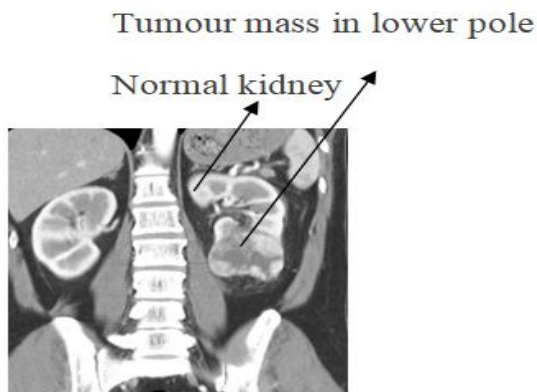


Figure 3: Renal cell cancer (RCC) lower pole of left kidney. Arterial (40sec) contrast enhanced phase.

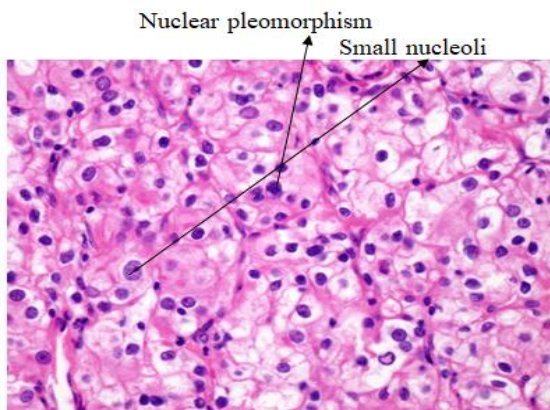


Figure 4: Section studied shows clear cell carcinoma with features of tumor cells have mild nuclear pleomorphism with occasional small nucleoli and stippled chromatin typical of Fuhrman grade 2 nuclei.

The histopathology and radiology correlation was perfect in all the cases. [Figure 1 and 2]

The histopathology and radiology correlation was perfect in all the cases. [Figure 3 and 4]

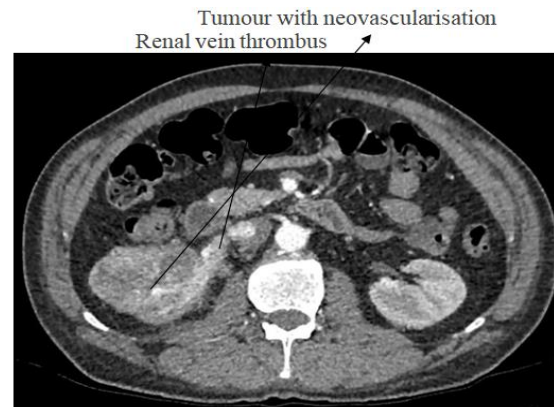


Figure 5: An arterial phase CT will show enhancement of a tumour thrombus due to neovascularisation of the tumour, as in this case.

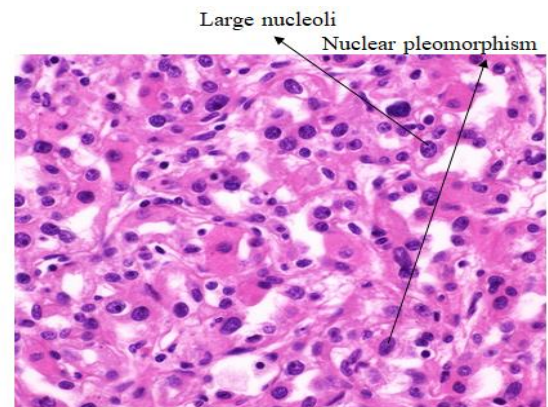


Figure 6: Section studied shows clear cell carcinoma with features of Fuhrman grade 3 nuclei, patchy, and show moderate pleomorphism and large nucleoli.

The histopathology and radiology correlation was perfect in all the cases. [Figure 5 and 6]



Figure 7: Left heterogenous enhancing mass in the mid-pole of the left kidney. This is well illustrated on this 4 phase renal angiogram CT study.

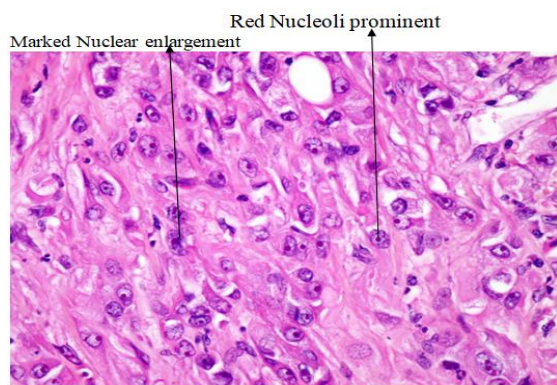


Figure 8: The marked nuclear enlargement of grade 4 nuclei is obviously seen. Prominent cherry-red nucleoli, with some nuclei harbouring two or three nucleoli

The histopathology and radiology correlation was perfect in all the cases. [Figure 7 and 8]

Papillary Renal Cell Carcinoma (PRCC):

Majority of tumours occur sporadically, but some may develop in members of families with hereditary. Papillary renal cell carcinoma arises from distal convoluted tubules can be multifocal and bilateral most common form in dialysis-associated RCC type I is sporadic, generally good prognosis type II is inherited, bilateral and multifocal. Microscopically type I have papillae covered by a single layer of cuboidal or low columnar cells with scanty cytoplasm and low-grade nuclei and carry a better prognosis than type II tumours. Microscopically type II are of a higher nuclear grade and contain more than one layer of cells with abundant eosinophilic cytoplasm. Six cases papillary cell renal carcinoma of were reported. Three cases involving females and three case involving males. The age group involved in females range from 60-74 years of age old and the age involved in male was 64-75 years of age old. Papillary Renal Cell Carcinoma, Type I

Tumour well circumscribed lesion
Extension to the calyceal system

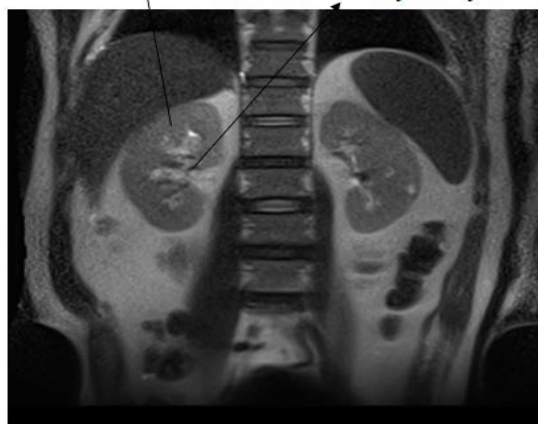


Figure 9: MRI scan shows a well circumscribed, 31mm diameter, lesion is identified along the supero-posterior cortical pole of the right kidney. It extends deep towards the calyceal system.

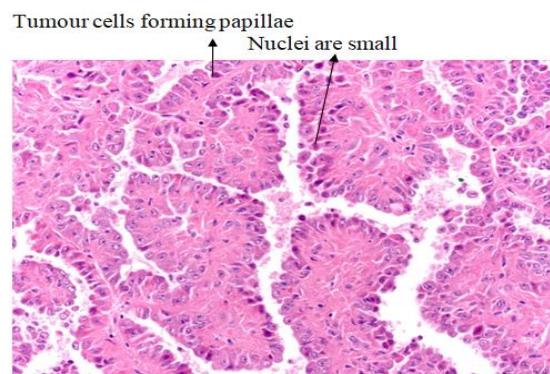


Figure 10: Section studied shows Renal Cell Carcinoma sub type papillary carcinoma with features of numerous papillae, the nuclei are small, and have open chromatin and indistinct nucleoli typical of type 1 papillary renal cell carcinoma.

The histopathology and radiology correlation was perfect in all the cases. [Figure 9 and10]

Renal cell carcinoma (type II papillary)

Tumour mass with heterogenous enhancement
Renal vein seen in phase 4 angiogram



Figure 11: Left heterogenous enhancing mass in the mid-pole of the left kidney. This is well illustrated on this 4 phase renal angiogram CT study.

Tumour cells forming tubulo papillary structures
Tumour cells showing nuclear enlargement

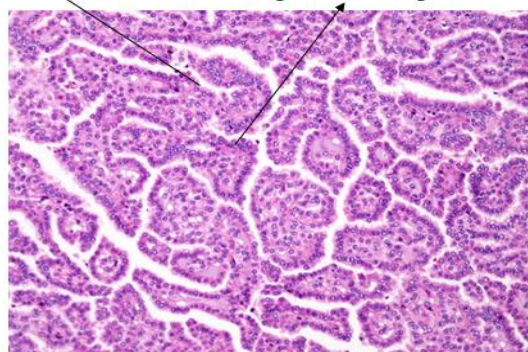


Figure 12: Section studied shows Renal Cell Carcinoma sub type papillary carcinoma a tumour composed of several tubulo-papillary structures. There is nuclear enlargement and hyperchromasia, prominent nucleoli and more abundant eosinophilic cytoplasm.

The histopathology and radiology correlation was perfect in all the cases. [Figure 11 and12]

Chromophobe Renal Cell Carcinoma: The frequency of incidence among overall renal cell carcinoma is Chromophobe is derived from the cortical collecting duct. Chromophobe renal cell carcinoma has a much better prognosis than clear cell and papillary renal cell carcinoma, with 5-year survival rate of greater than 90%. Most cases arise sporadically, while some familial cases are associated with Birt–Hogg–Dube (BHD) syndrome. Microscopically the neoplastic cells have a fine reticular cytoplasm and bland nuclei some of which have 'raisinoid' appearance. The cells have distinct, thick nuclear membranes and perinuclear halos. Some cells have no nuclei in the plane of section due to the voluminous cytoplasm. This renal cell carcinoma arises from intercalated cells of collecting ducts, similar histologically to renal oncocytomas best prognosis. Three cases were reported. The age group involved in two females range from 62-70 years of age old and the age involved in male was 75 years of age old.

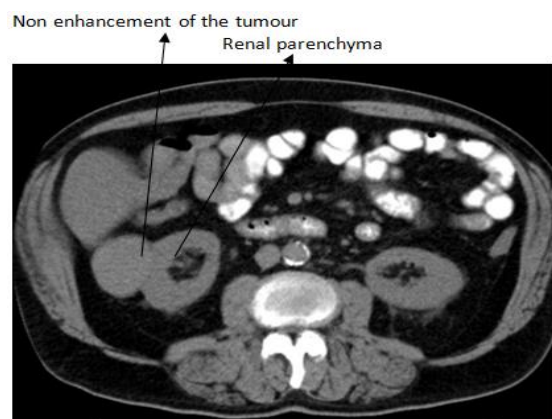


Figure 13: CT shows a 5 cm right renal mass lesion isodense to renal parenchyma. Weak contrast enhancement from 40 to 50 HU on the average.

The histopathology and radiology correlation was perfect in all the cases. [Figure13 and 14].

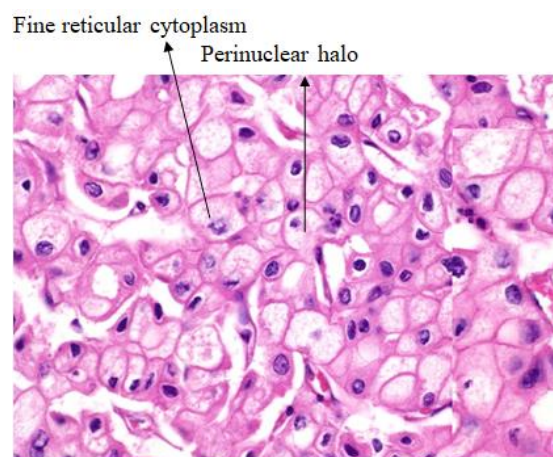


Figure 14: Section studied shows the neoplastic cells have a fine reticular cytoplasm and bland nuclei some of which have 'raisinoid' appearance. The cells have distinct, thick nuclear membranes and perinuclear halos.

Metastatic renal cell carcinoma

The most common sites for metastasis are the lymph nodes, lung, bones, liver and brain. Average survival time in 2008 for the metastatic form of the disease was under a year and by 2013 this improved to an average of 22 months. From 2007 to 2013, seven new treatments have been approved specifically for metastatic RCC (sunitinib, temsirolimus, bevacizumab, sorafenib, everolimus, pazopanib and axitinib). These new treatments are based on the fact that renal cell carcinomas are very vascular tumors – they contain a large number of blood vessels. The drugs aim to inhibit the growth of new blood vessels in the tumors, hence slowing growth and in some cases reducing the size of the tumors. Paraneoplastic syndromes are seen in about 25% of RCC patients will develop a paraneoplastic syndrome. They are hypercalcaemia (20%), hypertension (20%), polycythaemia: from erythropoietin secretion (~5%), Stauffer syndrome: hepatic dysfunction not related to metastases, feminisation, limbic encephalitis.

Table 5: Final Outcome of the Study

The prognosis is influenced by several factors, including tumour size, degree of invasion and metastasis, histologic type, and nuclear grade. The papillary renal cell carcinoma and chromophobe renal cell carcinoma responded moderately to the treatment. The clear cell renal carcinoma did not respond to treatment to the expected mark.

Tumour	Surgery Done	Cure rate measured after 3 years	Follow up
Clear cell renal carcinoma	Ten cases were stage I. Four cases were stage II. Two cases were stage III. Partial nephrectomy was done treatment for RCC tumors of less than 4 cm in diameter. Partial nephrectomy or radical nephrectomy was done for stage Ib tumors. Radical nephrectomy be performed for stage II and III tumors.	75 %	Eleven cases attend regular follow up. One case died of multiple organ failure.
Papillary renal cell carcinoma	Three cases were stage I. Two cases were stage II. One case was in stage III. Partial nephrectomy was done treatment for RCC tumors of less than 4 cm in diameter. Partial nephrectomy or radical nephrectomy was done for stage Ib tumors. Radical nephrectomy be performed for stage II and III tumors.	50%	Three cases are attending the follow up.
Chromophobe renal cell carcinoma	One case were stage I. Two cases were stage II. Partial nephrectomy was done treatment for RCC tumors of less than 4 cm in diameter. Radical nephrectomy was done for stage Ib tumors. Radical nephrectomy be performed for stage II.	66%	Two cases are attending the follow up.

Baseline abdominal CT or MRI within 3-6 months, then CT, MRI or US every 3-6 months for at least 3 years and then annually up to 5 years; baseline chest CT within 3-6 months after surgery with continued imaging (CT or chest X-ray) every 3-6 months for at least 3 years and then annually up to 5 years.

DISCUSSION

Renal cell carcinoma in our study, the common subtypes were clear cell renal cell carcinoma, papillary renal cell carcinoma and chromophobe renal cell carcinoma, were the common subtypes observed. The papillary renal cell carcinoma and chromophobe renal cell carcinoma responded moderately to the treatment. The total cases reported in the department is twenty five cases out of which sixteen cases are attending follow up after 3 years. The clear cell renal carcinoma did not respond to treatment to the expected mark. RCC is not a single uniform entity but a group of related neoplasms in which the histologic findings, cytogenetic abnormalities, biologic behaviour and imaging appearances of the tumors are subtype dependent. The 3 main subtypes - clear cell, papillary and chromophobe - can often be differentiated non-invasively based on characteristic radiologic appearances. Based on the hypothesis, that the diffusion of water to and from the cells is highly dependent on the ratio of intracellular and extracellular space, DWI MRI Scan is used to differentiate the tumour grades. Organ-sparing treatment can be entertained in selected cases. This ranges from adrenal sparing nephrectomy to partial nephrectomy, performed both open or laparoscopically. Additionally, percutaneous radiofrequency or cryoablation (typically under CT guidance), which can be carried out with only local anaesthetic and sedation, has been introduced in selected cases. Avastin is a targeted therapy that blocks a protein known as VEGF. Votrient is a targeted oral medication known as an angiogenesis inhibitor. Sutent is an oral multitargeted tyrosine kinase inhibitor that targets proteins responsible for stimulating cancer cell growth. 5-Fluorouracil (5FU) appears to be the most effective chemotherapeutic agent currently available for kidney cancer.

CONCLUSION

Imaging remains the primary tool for the detection and screening of RCC. Perfusion MRI and diffusion MRI play important roles in tumor characterization, prediction, and early detection of therapeutic response and used to differentiate the histology of renal masses in some preliminary studies. Dynamic contrast-enhanced (DCE) DCE and Perfusion MRI can also be used to estimate the morphologic grading of renal cell carcinoma. Histopathology provided the final diagnosis. The prognostic significance of tumor

necrosis in clear cell RCC has been confirmed by other groups. More aggressive RCC tumors, which are likely to exhibit necrosis, also harbor increased numbers of tumor infiltrating T cells. Tumor necrosis has garnered increasing attention over the last few years, in part because a number of studies have now shown that tumor necrotic tissues can be successfully targeted to facilitate both external tumor imaging and to foster a therapeutic antitumoral response by the host. Coagulative tumor necrosis represents a significant prognostic marker for clear cell and chromophobe RCC. The landscape for renal cell carcinoma treatment has changed dramatically in recent years, with the addition of three new FDA-approved agents this year. This brings our arsenal to seven drugs: interleukin-2, the VEGF receptor TKI's sunitinib, sorafenib, and pazopanib, the VEGF neutralizing antibody bevacizumab in combination with interferon, and the mTOR inhibitors temsirolimus and everolimus. Preoperative radiological classification can be used as a supplement to the histopathological grading. The study provides the importance of other medical faculty the Surgeon, Radiologist and Oncologist to work as a team for a successful outcome. We correlated the Histopathological findings with Radiological findings. This resulted in perfect correlation between the Histopathology study and Radiology study.

REFERENCES

1. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Lyon: IARC Press; 2004.
2. Motzer RJ, Agarwal N, Beard C, Bhayani S, Bolger GB, Carducci MA, Chang SS, Choueiri TK, Hancock SL, Hudes GR, et al. Kidney cancer. J Natl Compr Canc Netw. 2011.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;125:231-248.
4. ?
5. Lopez-Beltran A, Carrasco JC, Cheng L, Scarpelli M, Kirkali Z, Montironi R. 2009 update on the classification of renal epithelial tumors in adults. Int J Urol. 2009.
6. Cheville JC, Lohse CM, Zincke H, Weaver AL, Blute ML. Comparisons of outcome and prognostic features among histologic subtypes of renal cell carcinoma. Am J Surg Pathol. 2003;
7. Moch H, Gasser T, Amin MB, Torhorst J, Sauter G, Mihatsch MJ. Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma: a Swiss experience with 588 tumors. Cancer. 2000.
8. Hoffmann NE, Gillett MD, Cheville JC, Lohse CM, Leibovich BC, Blute ML. Differences in organ system of distant metastasis by renal cell carcinoma subtype. J Urol. 2008.
9. Beck SD, Patel MI, Snyder ME, Kattan MW, Motzer RJ, Reuter VE, Russo P. Effect of papillary and chromophobe cell type on disease-free survival after nephrectomy for renal cell carcinoma. Ann Surg Oncol. 2004.
10. Amin MB, Corless CL, Renshaw AA, Tickoo SK, Kubus J, Schultz DS. Papillary (chromophil) renal cell carcinoma:

- histomorphologic characteristics and evaluation of conventional pathologic prognostic parameters in 62 cases. *Am J Surg Pathol*. 1997.
11. Gurel S, Narra V, Elsayes KM, Siegel CL, Chen ZE, Brown JJ. Subtypes of renal cell carcinoma: MRI and pathological features. *Diagn Interv Radiol*. 2013
12. F, Kuroda N, Beothe T, Kaur AP, Kovacs G. Deletion of chromosome 3p14.2-p25 involving the VHL and FHIT genes in conventional renal cell carcinoma. *Cancer Res*. 2003 .
13. Lubensky IA, Schmidt L, Zhuang Z, Weirich G, Pack S, Zambrano N, Walther MM, Choyke P, Linehan WM, Zbar B. Hereditary and sporadic papillary renal carcinomas with c-met mutations share a distinct morphological phenotype. *Am J Pathol*. 1999.
14. Jones TD, Eble JN, Cheng L. Application of molecular diagnostic techniques to renal epithelial neoplasms. *Clin Lab Med*. 2005.
15. Prasad SR, Humphrey PA, Catena JR, Narra VR, Srigley JR, Cortez AD, Dalrymple NC, Chintapalli KN. Common and uncommon histologic subtypes of renal cell carcinoma: imaging spectrum with pathologic correlation. *Radiographics*. 2006.
16. Amin MB, Amin MB, Tamboli P, Javidan J, Stricker H, dePeralta Venturina M, Deshpande A, Menon M. Prognostic impact of histologic subtyping of adult renal epithelial neoplasms: an experience of 405 cases. *Am J Surg Pathol*. 2002 ,
17. Young JR, Margolis D, Sauk S, Pantuck AJ, Sayre J, Raman SS. Clear cell renal cell carcinoma: discrimination from other renal cell carcinoma subtypes and oncocytoma at multiphasic multidetector CT. *Radiology*. 2013.
18. Choueiri TK, Plantade A, Elson P, Negrier S, Ravaud A, Oudard S, Zhou M, Rini BI, Bukowski RM, Escudier B. Efficacy of sunitinib and sorafenib in metastatic papillary and chromophobe renal cell carcinoma. *J Clin Oncol*. 2008.
19. Tannir NM, Thall PF, Ng CS, Wang X, Wooten L, Siefker-Radtke A, Mathew P, Pagliaro L, Wood C, Jonasch E. A phase II trial of gemcitabine plus capecitabine for metastatic renal cell cancer previously treated with immunotherapy and targeted agents. *J Urol*. 2008.
20. Vikram R, Ng CS, Tamboli P, Tannir NM, Jonasch E, Matin SF, Wood CG, Sandler CM. Papillary renal cell carcinoma: radiologic-pathologic correlation and spectrum of disease. *Radiographics*. 2009.
21. Upton MP, Parker RA, Youmans A, McDermott DF, Atkins MB. Histologic predictors of renal cell carcinoma response to interleukin-2-based therapy. *J Immunother*. 2005.
22. Motzer RJ, Jonasch E, Agarwal N, Beard C, Bhayani S, Bolger GB, Chang SS, Choueiri TK, Costello BA, Derweesh IH, et al. Kidney cancer, version 3.2015. *J Natl Compr Canc Netw*. 2015.
23. Zhang J, Lefkowitz RA, Bach A. Imaging of kidney cancer. *Radiol Clin North Am*. 2007.
24. Prando A, Prando D, Prando P. Renal cell carcinoma: unusual imaging manifestations. *Radiographics*. 2006.
25. Park SB, Cho KS, Lee JH, Jeong YK, Choi SH, Kang BS, Kim JK. Unusual manifestations of renal cell carcinoma. *Acta Radiol*. 2008.
26. Sun MR, Ngo L, Genega EM, Atkins MB, Finn ME, Rofsky NM, Pedrosa I. Renal cell carcinoma: dynamic contrast-enhanced MR imaging for differentiation of tumor subtypes--correlation with pathologic findings. *Radiology*. 2009.
27. Campbell N, Rosenkrantz AB, Pedrosa I. MRI phenotype in renal cancer: is it clinically relevant? *Top Magn Reson Imaging*. 2014.
28. Ramamurthy NK, Moosavi B, McInnes MD, Flood TA, Schieda N. Multiparametric MRI of solid renal masses: pearls and pitfalls. *Clin Radiol*. 2015.
29. Lee-Felker SA, Felker ER, Tan N, Margolis DJ, Young JR, Sayre J, Raman SS. Qualitative and quantitative MDCT features for differentiating clear cell renal cell carcinoma from other solid renal cortical masses. *AJR Am J Roentgenol*. 2014.
30. Breda A, Lucarelli G, Rodriguez-Faba O, Guirado L, Facundo C, Bettocchi C, Gesualdo L, Castellano G, Grandaliano G, Battaglia M, et al. Clinical and pathological outcomes of renal cell carcinoma (RCC) in native kidneys of patients with end-stage renal disease: a long-term comparative retrospective study with RCC diagnosed in the general population. *World J Urol*. 2015.
31. Shrewsbury AB, Osunkoya AO, Jiang K, Westby R, Canter D, Pattaras J, Turgeon N, Master VA, Ogan K. Renal cell carcinoma in patients with end-stage renal disease has favorable overall prognosis. *Clin Transplant*. 2014.
32. Neuzillet Y, Tillou X, Mathieu R, Long JA, Gigante M, Paparel P, Poissonnier L, Baumert H, Escudier B, Lang H, et al. Renal cell carcinoma (RCC) in patients with end-stage renal disease exhibits many favourable clinical, pathologic, and outcome features compared with RCC in the general population. *Eur Urol*. 2011.
33. Byler TK, Bratslavsky G. Hereditary renal cell carcinoma: genetics, clinical features, and surgical considerations. *World J Urol*. 2014.
34. Rosner I, Bratslavsky G, Pinto PA, Linehan WM. The clinical implications of the genetics of renal cell carcinoma. *Urol Oncol*. 2009.
35. Lonser RR, Glenn GM, Walther M, Chew EY, Libutti SK, Linehan WM, Oldfield EH. von Hippel-Lindau disease. *Lancet*. 2003.
36. Byler TK, Bratslavsky G. Hereditary renal cell carcinoma: genetics, clinical features, and surgical considerations. *World J Urol*. 2014.
37. Ricketts CJ, Shuch B, Vocke CD, Metwalli AR, Bratslavsky G, Middleton L, Yang Y, Wei MH, Pautler SE, Peterson J, et al. Succinate dehydrogenase kidney cancer: an aggressive example of the Warburg effect in cancer. *J Urol*. 2012 .
38. Ricketts CJ, Shuch B, Vocke CD, Metwalli AR, Bratslavsky G, Middleton L, Yang Y, Wei MH, Pautler SE, Peterson J, et al. Succinate dehydrogenase kidney cancer: an aggressive example of the Warburg effect in cancer. *J Urol*. 2012
39. Escudier B, Eisen T, Porta C, Patard JJ, Khoo V, Algaba F, Mulders P, Kataja V. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2012.
40. Bellmunt J, Puente J, Garcia de Muro J, Lainez N, Rodríguez C, Duran I. SEOM clinical guidelines for the treatment of renal cell carcinoma. *Clin Transl Oncol*. 2014 .
41. Krabbe LM, Bagrodia A, Margulis V, Wood CG. Surgical management of renal cell carcinoma. *Semin Intervent Radiol*. 2014.
42. Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MA. The natural history of incidentally detected small renal masses. *Cancer*. 2004.
43. Serum and urine biomarkers for human renal cell carcinoma. *Dis Markers*. 2015.
44. Lee CT, Katz J, Fearm PA, Russo P. Mode of presentation of renal cell carcinoma provides prognostic information. *Urol Oncol*. 2002 .
45. Pedrosa I, Chou MT, Ngo L, H Baroni R, Genega EM, Galaburda L, DeWolf WC, Rofsky NM. MR classification of renal masses with pathologic correlation. *Eur Radiol*. 2008.
46. Muglia VF, Prando A. Renal cell carcinoma: histological classification and correlation with imaging findings. *Radiol Bras*. 2015.
47. Kim JK, Kim TK, Ahn HJ, Kim CS, Kim KR, Cho KS. Differentiation of subtypes of renal cell carcinoma on helical CT scans. *AJR Am J Roentgenol*. 2002.
48. Pedrosa I, Alsop DC, Rofsky NM. Magnetic resonance imaging as a biomarker in renal cell carcinoma. *Cancer*. 2009.
49. Yoshimitsu K, Irie H, Tajima T, Nishie A, Asayama Y, Hirakawa M, Nakayama T, Kakiyama D, Honda H. MR

imaging of renal cell carcinoma: its role in determining cell type. Radiat Med. 2004

50. Oliva MR, Glickman JN, Zou KH, Teo SY, Mortel AJ, Rocha MS, Silverman SG. Renal cell carcinoma: t1 and t2 signal intensity characteristics of papillary and clear cell types correlated with pathology. AJR Am J Roentgenol. 2009.
51. Goyal A, Sharma R, Bhalla AS, Gamanagatti S, Seth A, Iyer VK, Das P. Diffusion-weighted MRI in renal cell carcinoma: a surrogate marker for predicting nuclear grade and histological subtype. Acta Radiol. 2012.
52. Choi YA, Kim CK, Park SY, Cho SW, Park BK. Subtype differentiation of renal cell carcinoma using diffusion-weighted and blood oxygenation level-dependent MRI. AJR Am J Roentgenol. 2014.
53. Wang H, Cheng L, Zhang X, Wang D, Guo A, Gao Y, Ye H. Renal cell carcinoma: diffusion-weighted MR imaging for subtype differentiation at 3.0 T. Radiology. 2010.
54. Lassel EA, Rao R, Schwenke C, Schoenberg SO, Michael HJ. Diffusion-weighted imaging of focal renal lesions: a meta-analysis. Eur Radiol. 2014.

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